REMARKS

1. Objections

Claims 1, 5 and 6 have been amended as suggested by the Examiner. The objection to 3 is moot as that claim has been cancelled.

2. Definiteness

1. The Examiner has questioned whether "over expressing the activity" (claim 1) refers to the level of expression (production) of the enzyme or the level of enzyme activity (for a given enzyme production level). Similar questions are raised with respect to claim 4.

Claims 1 and 4 have been amended to clearly refer to the level of expression. Of course, total enzyme activity should be proportional to enzyme levels, but we have not required any alteration of the enzymatic potency of the enzyme molecules.

2. The Examiner questions whether claim 9 intends an increase in the rate (speed) of uptake or the level of uptake. Claim 9 recites "an increase of... uptake rate" and it means exactly what it says; claim 9 clearly refers to an increase in rate of uptake.

The examiner also questions the meaning of "specific galactose uptake rate in claim 9", as well as "specific ethanol production rate" in claim 11. The general usage of "specific" is to imply division by a count, mass or volume, i.e., to normalize the value in question.

The term 'specific galactose uptake rate' (claim 9) would be well understood by those skilled in the art; it is not ambiguous. It means the speed with which the nutrient (galactose) is taken up, corrected for the amount of the micro-organism present. This is further apparent from for instance the table on page 14 where it is measured in units of 'g galactose/g dry weight/hour'.

The Examiner objects that it is unclear whether certain specific conditions must be used in determining whether the rate

is higher for the recombinant organism compared to the reference. Clearly, the comparison should be like for like, i.e. the same conditions should be used for the recombinant organism and for the reference organism and they should be conditions under which both organisms grow, but beyond that it is not necessary to specify conditions. There is no basis for suggesting that the outcome of the test is dependent on the selection of special conditions.

The phrase 'specific ethanol production rate' would be understood by those skilled in the art; it is not ambiguous. It means the speed with which the ethanol is produced, corrected for the amount of the micro-organism present. This is further apparent from for instance the table on page 14 where it is measured in units of 'g ethanol/g dry weight/hour'.

The Examiner enquires whether any measurement of ethanol production will suffice. Since the measurement is a relative one, the result will be unaffected by the choice of weight measuring system or time units.

Claims 9-12 and 17 have been amended to explicitly state what is measured in the reference microorganism (although we think it was previously implicit).

The "reference micro-organism" of claims 9-12 is the same as the one in claim 1. We have amended the claims accordingly.

In particular, reference to 'a said reference micro-organism' has been changed to 'said reference micro-organism', as suggested.

3. Written Description

Another new rejection is of claims 1-6 and 8-12, for lack of adequate written description of either the enzyme or the fungus. The Examiner concedes disclosure of the enzymes PGM1 and PGM2, and of three preferred species (S. cerevisiae, P. pastoris, A. niger).

The issue, as framed by the Examiner, is whether the disclosed species are representative of the claimed genus (any

enzyme catalyzing the conversion of glucose-1 phosphate to glucose-6-phosphate; any prototrophic fungus).

The Examiner has commented in support of this rejection, at page 7, last paragraph of the official action, that the claims 'do not provide any structural information with regard to the enzymatic sequences capable of catalyzing the conversion of glucose-1 phosphate to glucose-6 phosphate...'.

By the present amendment, the enzyme is restricted now to PGM2, an enzyme of completely known structure.

Secondly, the Examiner has objected that the claims are not restricted to any species of fungi. However, the biochemical pathway which is being manipulated according to the invention is a fundamental one which is common to fungi in general. (It is also noted that the objection has been raised against claim 2, in which the fungi is specified to be a yeast.)

With respect to the discussion by the Examiner of the exemplification of the invention, the Examiner has stated that the example 'is not necessarily predictive of any other enzyme, wild type or mutant, capable of catalyzing the conversion of glucose-1 phosphate to glucose-6 phosphate.

We submit that 'not necessarily predictive' is not an appropriate standard to apply. The Applicant has provided a reasoned written account of how the invention works which is based on an understanding of the details of a fundamental biochemical pathway. The Applicant has successfully predicted that the outcome of the exemplified modification of their chosen starting organism, and has demonstrated the correctness of their prediction.

The Examiner has put forward no specific reason why the invention should not operate in other yeasts, and other fungi in general. We submit that the rejection should be withdrawn.

4. Enablement

There is a somewhat parallel enablement rejection. There, however, the Examiner explicitly concedes enablement for wild

type PGM2 in S. cerevisiae.

The Examiner acknowledges that four enzymes (AGM, PGM1, PGM2, and PMM) are known to catalyze the critical conversion, but argues that only one is known to result in a fungus with increased galactose/ethanol uptake. For the reasons already put forth in connection with written desription, we submit that the enablement rejection under this heading in respect of alleged lack of enablement should be withdrawn also.

5. Prior Art

The Examiner has rejected claims 1-6 and 8-12 as anticipated by Weinstock et al (US 6747137). It is alleged that Weinstock et al discloses a recombinant fungal cell transformed with SEQ ID NO 2964 which encodes phophoglucomutase 2. It is suggested that it is inherent in such a proposition that the transformed fungal cell will exhibit increased galactose uptake when cultured on a nutrient source providing galactose.

We submit that the rejection is in error and should be withdrawn.

It will be appreciated that there is no actual disclosure in Weinstock et al of any specific fungal strain in which the said sequence is expressed. Accordingly, no properties of such a strain are determined and described. Neither are there any instructions in Weinstock et al which relate in particular to the said sequence and which would provide specific instructions as to how that particular sequence should be expressed. There are some 14103 sequences in Weinstock et al, and there may be different conditions relevant to the expression of different ones of them.

Weinstock et al is directed to the task of elucidating the genome of C. albicans with a view to better combating fungal infection (Col 2, lines 36 - 44). To this end, Weinstock et al propose fragmenting the genome of C. albicans, so generating sequences SEQ ID NO 1-14103. There are general instructions to express C. albicans polypeptides in host organisms. The host

cells may be fungal (Col 8, line 28). The Examiner refers to column 22. There it is disclosed that to find the function of a specific gene, it may be expressed in a fungal strain. It is said that:

> 'The function of a specific gene or operon can be ascertained by expression in a fungal strain under conditions where the activity of the gene products specified by the gene or operon in question can be specifically measured. ... This expression can be accomplished in a mutant strain that lacks the activity of the gene to be tested, or in a strain that does not produce the same gene product(s). This includes, but is not limited to, Eucaryotic species such as the yeast Saccaromyces cerevisiae or Candida putida, Methanobacterium strains or other Archaea, and Eubacteria such as E. coli, B. subtilis, S. aureus, S. pneumonia or Pseudomonas putida.'

Thus, it can be seen that there is no instruction to express SEQ ID NO 2964 in a yeast. The reader has to make their own choice of organism in which they will express that particular sequence. There is however guidance for their selection of organism in the teaching that it is a 'a strain that does not produce the same gene product(s)'.

It is evident that for different C. albicans gene products, different host organisms will better satisfy the stated requirements. In particular, contrary to the Examiner's reasoning, nowhere is it taught that the organism in which SEQ ID NO 2964 should be expressed should be fungal, should be Saccharomyces cerevisiae or should be Candida putida. In so far as Weinstock et al contains teaching on the micro-organism in which to express SEQ ID NO 2964, it teaches away from these organisms towards organisms in which PGM2 is not native.

In our submission, it is improper to raise an objection requiring the finding of certain properties to be inherent when

there is no unambiguous teaching of a relevant particular recombinant organism for which the properties can be ascertained.

Thus, it is fundamentally insufficient for the Examiner to hypothesise regarding the result of putting the C. albicans sequence SEQ ID NO 2964 into Saccharomyces cerevisiae, because whether the Examiner is right or wrong regarding the properties that would result, there is no teaching in Weinstock et al to make specifically such a recombinant organism.

That is just one possible result out of all the other possible results arising from the expression of Weinstock et al's 14,000 sequences in at least seven named possible hosts.

Moreover, given the aim in Weinstock et al to discover the function of polypeptides in C. albicans , this is a particularly inappropriate combination to make as the function of PGM2 was already known. There would therefore be no rational motive for making this specific combination.

The Examiner refers to columns 43 and 44. There is discussion there of 'Overexpression assays' and 'Ligand binding assays'. As is explained there, these are to find C. albicans polypeptides that are relevant for finding compounds that interfere selectively with the function of a gene product polypeptide. There is no teaching in Weinstock et al that SEQ ID NO 2964 is a suitable sequence against which to direct such assays. In so far as phophoglucomutase 2 is a previously known widely occurring enzyme, it would not be seen by the skilled reader as a sequence to which this particular teaching was of much relevance. Clearly, the polypeptides that lend themselves to use in such screens are ones that are specific to C. albicans (rather than being widely distributed in nature, as only polypeptides specific to C. albicans can lead to the development of medicaments that target C. albicans.

Once again, we see that there is no specific teaching to over express SEQ ID NO 2964 in any organism, much less in S. cerevisiae and no clear motivation is provided that would make this an obvious choice.

Respectfully submitted,

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